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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,401	PAGES, JEAN-CHRISTOPHE	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2009* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are pending. Claims 9 and 11 have been amended and are now under examination in the present action.

Applicants' amendment to correct the drawings is sufficient to overcome the objection to the drawings. However, applicants have neither amended the specification nor addressed the following issues in their arguments. In lieu of a Non-Responsive Notice, the objections are set forth again.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, page 6, line 22 and 24, page 10, line 26 and 30, page 11, line 15 and figure 2 contain sequences that are not identified by sequence identifier numbers. If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:s. If not, a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, CRF and letter stating that the contents of the sequence listing and the CRF are the same and contain no new matter is required. **The nature of the non-compliance did not preclude the examination on the merits of the instant application, the results of which follow.**

Specification

The disclosure is objected to because the use of the trademarks throughout the specification has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 1-8, 10 and 12-24 are objected to because of the following informalities: **This objection is restated from the action mailed 4/8/09.**

Claims 2-8 and 13-24 require articles at the beginning of each claim. Independent claims should use the article "a" or "an" and dependent claims "the". Applicants have amended the dependent claims incorrectly by adding the article "a" instead of --the--.

Appropriate correction is required.

These are new objections. For proper antecedent basis to be established, the phrase "alphavirus vector" in claim 1, line 2 should be amended to --alphavirus genome vector--. As well, *in all of the claims the recitation* "the genome of the alphavirus-derived vector" should be amended to correct recitation of "derived" and to establish antecedent basis should be amended to --the alphavirus genome vector--.

In claims 4 and 20, the recitation "the alphavirus" can refer to either the vector or the alphavirus from which the structural proteins cannot come. It is noted that these alphavirus need not be the same source. Hence, claims 4 and 20 recite either that the genome vector is Semliki forest virus or else the structural proteins are not from SFV. However, it is not clear which. If it is the later, it would be remedial to recite, --the alphavirus genome vector--.

For clarification in claim 12, line 4 "consisting" should be amended to --wherein the method consists of--. Recitations of derived in claim 12 should be amended to --obtained--.

Throughout the claims the phrase "characterized in that" should be amended to --wherein-- as the phrase characterized does not carry any requirement that the elements have a direct relationship. Rather by being characterized, the limitations can be only vaguely related. Similarly, use of "correspond to" in claims 3, 16 should be amended to --consists of--.

In claim 14, the phrase "characterized in that the expression in trans is obtained by cotransfection" requires clarification by amendment to --wherein the expression in trans comprises cotransfection--. This amendment corrects use of "characterized in that" but also expression is not obtained but it the inherent consequence of cotransfection. Similarly, claims 17, 18 and 19 should be amended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9-20, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Dubensky et al (US 5,843,723; see entire document). **This rejection is maintained for reasons of record in the office action mailed 4/8/09 and restated below. The rejection has been extended to newly rejoined claims 9 and 11.**

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15. A translation of PCT/JP03/04553 is also required to ascertain that the designation that this application is a continuation of JP 2002-108550.

Dubensky et al teach a pseudotyped alphavirus comprising retrovirus envelope. As depicted in figure 8, the vector sequences are deleted of the structural genes which are replaced by at least one transgene. According to the claims such a virus would be replication defective, "vector made replication defective by deletion or replacement with at least one transgene, of the structural gene". Furthermore, the alphavirus is grown in a packaging cell line expressing VSV-G (see col 6, line 4-30 and col 96, line 18-39). Pharmaceutical compositions are taught (see col 48). The alphavirus psi region is deleted and replaced with that from retrovirus (see e.g. col 98, line 17-33). Methods of producing the viruses are taught (see e.g. col 96, line 40- col 98, line 33). For example, packaging cell lines expressing gag/pol and env are provided (see e.g. col 3, line 28-38). The cells can be 293 cells (see e.g. col 94, line 6-13). Retroviral-based particles containing alphavirus vector RNA are produced by transfecting in vitro transcribed alphavirus vector RNA using procedures that have been described previously. Supernatants with pseudotyped retroviral particles containing alphavirus RNA vector are harvested at 24 hours post-transfection, and these supernatants are then used to transduce an alphavirus packaging cell

line (col 98, line 26-36). These lines can comprise stably expressing gag/pol (see claim 45). Based upon the definition of encapsidation cell lines, the cells of Dubensky meet requirements of such cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky et al (US 5,843,723; see entire document) in view of Kung et al (see J Vi, 2000, pp 3668-3681; see entire document) or Raju et al, (JVi, 1991, Vol 65(5), pages 2501-2510; see entire document). **This rejection is maintained for reasons of record in the office action mailed 4/8/09 and restated below. The rejection has been extended to newly rejoined claims 9 and 11.**

Applicants claim a viral particle consisting of structural elements not from an alphavirus and containing an alphavirus vector made replication-defective by deletion or replacement with at least one transgene of the structural genes. The vector has a mutated p26S promoter and contains an extended packaging sequence of MLV vectors.

The teachings of Dubensky et al are described above and are applied as before except;

Dubensky et al do not teach that the vector has a mutated p26S promoter and contains an extended packaging sequence of MLV vectors.

Kung et al teach pseudotyping of lentivirus using MLV env protein VSV-G1. The vector incorporates the MLV extended packaging sequence, essential for the increase in retrovirus vector titers and gene transfer efficiency (see e.g. page 3669, ¶ 5). Kung et al teach a novel, unappreciated feature of this extended packaging sequence in gene expression. First, the extended packaging sequence stabilizes the mRNA transcript and therefore allows higher gene expression. Second, it may allow higher gene expression through a more efficient mRNA nuclear export.

Raju et al teach construction and use of mutant 26S promoters which alter the activity level of the promoter. Hence, higher and les activity can be provided by altering the mutant or wild-type promoter used (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the MLV extended packaging system as taught by Kung et al and the mutant 26S promoter as taught by Raju et al with the alphavirus vector expression system as taught by Dubensky et al because Kung et al teach that the extended packaging system can be used in vectors for production of pseudotyped particles and because Raju et al teach that the mutant 26s promoters can be used to express heterologous proteins. One would have been motivated to do so in order to receive the expected benefit of improved particle expression as well as improved protein expression. Furthermore, the combination of references demonstrates that it would be within skill of the art to use well known promoters in well known systems with predictable results. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Amendment

Applicants arguments filed 10/8/09 have been considered but are not persuasive for the following reason. Dubensky et al is explicitly drawn to a pseudotyped alphavirus. More specifically, Dubensky et al teaches use of VSV-G packaging cells that express VSV-G protein. This is explicitly an alphavirus vector comprising an envelope or structural protein that is not from alphavirus. "The generation of VSV-G pseudotyped alphavirus vector particles can be accomplished by at least three alternative approaches, two of which are dependent on the stable integration of a VSV-G expression cassette into cells." Hence, the alphavirus does not express the structural proteins of an alphavirus but does from, an alternative virus. Figure 8 so describes a vector without structural alphavirus proteins, "Within one aspect of the present invention, alphavirus vector constructs are provided comprising a 5' promoter which is capable of initiating the synthesis of viral RNA in vitro from cDNA, a 5' sequence which is capable of initiating transcription of an alphavirus, a nucleotide sequence encoding alphavirus non-structural proteins, a viral junction region which has been inactivated such that viral transcription of the subgenomic fragment is prevented, and an alphavirus RNA polymerase recognition sequence." Alphaviral structural proteins are translated from the subgenomic 26S RNA. The subgenomic fragment expression is prevented here and therefore the vector does not express alphavirus structural proteins.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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